REMARKS/ARGUMENTS

I. Status of the Claims

Claims 15 and 19 are amended. Claims 33 and 34 are added. Thus, claims 15 and 17-34 are pending with entry of this Amendment.

II. Status of the Claims

The amendments find support in the specification, drawings and claims as originally filed. For example, support for "thermostable" can be found on, e.g., on page 2, last full paragraph of the specification. Support for new claim 33 can be found on, e.g., page 3 in the fourth full paragraph of the specification. Support for new claim 34 can be found on, e.g., Example 5 on pages 15-16 of the specification. No new matter is added.

III. Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 15 and 17-32 as allegedly indefinite for reciting the phrases "suitable for PCR" and "wild-type form of a mutant polymerase." As amended, neither phrase is used in the claims. Accordingly , Applicants respectfully request withdrawal of the rejection.

Applicants note that the term "thermostable" was rejected as indefinite in paper no. 6. As noted previously by the Applicants (e.g., in the Amendment filed on March 14, 2002), one of skill in the art would readily understand what the term "thermostable" means in the context of DNA polymerases and in view of the specification. The term "thermostable polymerase" is commonly used in the art and is understood to mean that the polymerase retains polymerase activity after cycling through temperatures standard in PCR, e.g., 94°C. Indeed, the first sentence of the "Description of the Invention" on page 2 of the specification states that: "[t]he subject of the present invention was to provide **thermostable** DNA polymerases exhibiting an improved performance in PCR." Applicants invite the Examiner to demonstrate that those of skill in the art have any other understanding of the term.

IV. Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 15 and 17-32 under 35 U.S.C. § 112, first paragraph as allegedly not complying with the written description requirement. Specifically, the Examiner argued that the specification did not place any limit on the number of nucleic acid or amino acid substitutions that may be encompassed and that specific information regarding attributes or variations was not provided in the application. Applicants respectfully traverse the rejection.

"The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.'" *Union Oil Co. v. Atlantic Richfield Co.*, Docket No. 99-1066 (Fed. Cir. 2000) *citing In re Gosteli*, 10 USPQ 2d 1614, 1618 (Fed. Cir. 1989) (brackets in original). Moreover, the Federal Circuit has held that "every species in a genus need not be described in order that a genus meet the written description requirement." *Utter v. Hiraga*, 6 USPQ 2d 1709, 1714 (Fed. Cir. 1989).

In *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), the Federal Circuit confirmed that every species in a genus need not be described. However, the Federal Circuit required that the specification provide "structural features commonly possessed by members of the genus that distinguish them from others" (Emphasis added). *Id.* Moreover, the Federal Circuit in *Eli Lilly* acknowledged that disclosure of a representative number of species within the claimed genus may provide written description for the genus. *See, Id.* at 1569. The specification provides both structural features of mutant polypeptides that distinguish the claimed polypeptides from others and provides a number of examples that are encompassed by the present claims, thereby meeting the test set forth by the Federal Circuit.

The claims at issue are directed to mutant polymerases at least 80% identical to SEQ ID NO:34 wherein the polymerases comprise a Y-GG/A amino acid motif between an N-terminal 3'-5' exonuclease domain and a C-terminal polymerase domain and wherein the tyrosine of the Y-GG/A amino acid motif is substituted with another amino acid. Applicants remind the Examiner that the present claims are **not** directed to a previously unknown class of

proteins but instead are directed to a well-characterized class of enzymes. As explained in the background section of the present application, the structural basis for the catalytic activities of polymerases was generally understood as of the filing date of the present application. These activities include the polymerase activity mediated by the polymerase domain and exonuclease activity mediated by the exonuclease domain. *See, e.g.*, page 1 of the present specification. Moreover, B-type polymerases were known to coordinate these two domains via a Y-GG/A motif. *See, id.* Furthermore, the crystal structure of a number of polymerases has been solved. *See, e.g.*, page 2 of the present specification. Thus, each of these well-characterized domains and motifs were well known as of the filing date and therefore those of skill in the art would have understood the structural basis for their functions. In view of the extensive literature describing the structure and functions of polymerases, Applicants assert that those of skill in the art would have readily recognized that the inventors were in possession of the full scope of the claimed invention. The Examiner does not appear to have questioned that those of skill in the art could have readily modified known polymerase to change the tyrosine of the Y-GG/A amino acid motif.

The Office Action further argues that the specification does not provide a representative number of species to describe the claimed genus. *See, e.g.*, page 4 of the Office Action. This is simply not true. Applicants direct the Examiner to the last paragraph of page 3 of the specification which notes that the art has recognized that B-type DNA polymerases exhibit a high degree of sequence homology. The specification then proceeds to list polymerases from eight additional *Thermococcus* and *Prococcus* species that could also be modified according to the claimed invention. *See, e.g.*, page 3 of the present specification. In view of the high homology of polymerases within these two genera, polymerases from additional *Thermococcus* and *Prococcus* species would also be within the scope of the present claims.

The discussion of these additional species within the scope of the claims provides more than merely eight additional examples of polymerases within the scope of the claims. For example, to analyze protein sequences, it was standard procedure of those of skill in the art to create sequence alignments. Alignment of the nine different naturally-occurring polymerases that were within the scope of the claims and provided in the specification provides guidance

regarding how the polymerase sequences can be varied while retaining activity. Those of skill in the art would have appreciated that it is likely that an amino acid from one exemplified polymerase could be replaced with the corresponding amino acid from another of the listed polymerases without significantly affecting function. Thus, the application provided significant guidance regarding the structure/function relationship of polymerases, thereby meeting the requirements set forth by the Federal Circuit.

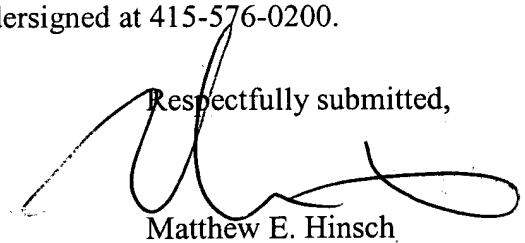
In consideration of the arguments above, applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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